III. Remarks

A. Amendments to the Claims

Applicants have amended claims 8–9, 13–16 and 20–21 to provide that the claimed suspension of particles of calcium salts are stabilized against agglomeration by a content of at least 0.01% by weight based on the weight of the suspension of a defined water-soluble polymeric protective colloid which, for claims 15–16, 20–21, 23 and 25 is limited to gelatin. In the remaining claims 8–9, 13–14, 22 and 24, the claimed colloid is selected from the group consisting of gelatin, casein, starch, plant gums, cellulose ethers, methylcellulose, hydroxyethylcellulose, carboxymethylcellulose, hydroxyethylstarch and hydroxypropylguar and is adsorbed onto said particles.

New claims 22–25 are directed to preferred embodiments of claims 13 and 14.

B. Rejection Under 35 U.S.C. Section 103

Claims 8–10, 13–17 and 20–21 are rejected under 35 U.S.C. Section 103(a) as being unpatentable over United States Patent No. 6,919,070 to Rudin et al., in view of United States Patent No. 4,098,878 to Baines et al.

1. The Examiner's reasons for the rejection

The Examiner's reasons for the rejection are set forth in the Action at page 2, lines 6–18 and are as follows:

> The primary reference has been discussed at length previously and differs from the instant claims insofar as it does not specify surface treatment of the inorganic particles (hydroxyapatite and other abrasives) contained in its dentifrice compositions.

> The secondary reference teaches that it is well-known to surface-treat inorganic particles (abrasives) in dentifrice compositions in order to improve their compatibility with potentially reactive components such as fluorides; in doing so, the particles are also stabilized against agglomeration. See column 6, lines 60–64. Surface treating agents include water-soluble surfactants (column 7, lines 30–34) which may be nonionic (column 3, lines 19–45). Although a variety of known abrasives are disclosed (column 8, lines 12–20), the secondary reference differs from the instant claims insofar as hydroxyapatites are not specifically mentioned.
>
> It would have been obvious to have surface-treated the hydroxyapatite particles of the primary reference with water-soluble surfactants, motivated by the desire to provide the improved compatibility taught by the secondary reference.

(Action, page 2, lines 6–18).

2. Legal standard for determining whether Applicants' claims are obvious under 35 U.S.C. Section 103

The legal interpretation of Section 103 to be applied is set forth in the recent Supreme Court decision of *KSR International Co. v. Teleflex Inc.* (*KSR*), 550 U.S. __, 82 USPQ2d 1385 (2007). *KSR* cites *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17–18 148 USPQ 459 (1966) as setting out an objective analysis for applying Section 103. (82 USPQ2d at 1388). The objective analysis is as follows:

> Under § 103, the scope and content of the prior art are to be determined; the differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, *etc.*, might be utilized to give light tot he circumstances surrounding the origin of the subject matter sought to be patented. As indicia of obviousness or nonobviousness, these inquiries may have relevancy.

(148 USPQ at 467).

Accordingly, the factual inquiries set forth by the Court are as follows:

(a) [T]he scope and content of the prior art are . . . determined;

(b) Differences between the prior art and the claims at issue are . . . ascertained;

(c) The level of ordinary skill in the prior art [is] resolved; and

(d) Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, *etc.*, might be utilized. . . .

3. Application of *Graham v. John Deere Co.*, factual standards

The application of the *Graham v. John Deere Co.* factual standards is being made in association with a Second Declaration of Dr. Christian Kropf, filed in Applicants' Amendment and Response dated August 22, 2007, and attached there and now as **EXHIBIT A** and a Third Declaration of Dr. Christian Kropf dated January 31, 2008, which is attached hereto as **EXHIBIT B**. Dr. Kropf is one of the inventors of the invention disclosed and claimed in this application.

(a) Determining the scope and content of the prior art

The Rudin et al. patent discloses a composition characterized in that it comprises particles of hydroxyapatite with an average particle size in length (l), width (d), and thickness (h). The values for these dimensions are: (l) from 0.2 μm to 0.01 μm, (d) 0.1 μm to about 0.001 μm and (h) from 0.1 μm to 0.0001 μm (column 2, lines 22–27) (Third Declaration of Christian Kropf, Paragraph 5).

Rudin et al. further discloses that the hydroxyapatite being introduced into the composition possesses osteo-reparative properties and contains preferably about 100% $Ca_{10}(PO_4)_6(OH)_2$ and that the specific surface of hydroxyapatite used in the composite advantageously is 100 to 150 m^2/g (column 2, lines 41–45). This disclosure indicates that the

hydroxyapatite disclosed in Rudin et al. is pure hydroxyapatite (Third Declaration of Christian Kropf, Paragraph 6).

Rudin et al. further discloses an oral product that will comprise a liquid phase containing humectants and binding thickeners which act to maintain the particulate solid abrasive and hydroxyapatite crystals in the form of stable suspension in liquid phase (column 3, lines 11–15). On the `basis of the disclosure in Rudin et al., the hydroxyapatite crystals in the suspension are pure hydroxyapatite (Third Declaration of Christian Kropf, Paragraphs 6 and 7).

The conclusion that the hydroxyapatite particles disclosed in Rudin et al. are pure is further based on the disclosure at column 2, lines 46–51 of Rudin et al. that U.S. Patent No. 6,254,855 B1 describes a method for producing a suspension of hydroxyapatite as described in the Rudin et al. application. U.S. Patent No. 6,254,855 B1 discloses in EXAMPLE 1 that according to the method described in that patent, a pure stochiometric hydroxylapatite in a suspension form is produced free of admixtures (column 3, lines 43–67) (Third Declaration of Christian Kropf, Paragraph 8).

The Baines et al. patent is directed to dentifrices containing as a dental abrasive, milled alpha-alumina trihydrate, which has been surface-treated with a higher fatty acid (Abstract) (Third Declaration of Christian Kropf, Paragraph 11).

As disclosed in Baines et al., milled alpha-alumina trihydrate tends (particularly when it is of a less alkaline type) to react with sodium fluoride. An analysis of freshly prepared toothpaste gives values of soluble fluoride much lower than when the abrasive is inert (column 1, lines 8–13) (Third Declaration of Kropf, Paragraph 12).

Baines et al. discloses that pre-treating the trihydrate with 1% stearic acid greatly inhibits the reaction of the trihydrate and the sodium fluoride (column 1, lines 24–29). This disclosure is further set forth in EXAMPLES 1 and 2 (column 1, line 35 to column 3, line 18) (Third Declaration of Christian Kropf, Paragraph 13).

Baines et al. further discloses as an objective the protection of the surfaces of the particles of abrasive in the dentifrice to reduce the chemical activity of the surfaces thereof, *e.g.*,

to prevent or hinder passage of components of the abrasive into the aqueous medium of the dentifrice. This protection is effected by means of a surface treatment with a water-insoluble material that adheres to active sites of said particles (column 6, lines 39–46). The particles may be maintained in substantially unagglomerated form (column 6, lines 60–61) (Third Declaration of Christian Kropf, Paragraph (14).

The treating materials may be any of the following:

- a waxy or high viscosity greasy material may be applied in a solvent (column 6, lines 50–51);
- polar materials including, for example higher (C_8–C_{22}) fatty alcohols and higher fatty acids, such as lauric and stearic acids and lauryl and stearyl and alcohol (column 7, lines 11–12 and 17–20);
- non-polar materials including waxes, vegetable oils such as palm oil and hydrogenated palm oil, and hydrocarbon oils and greases, *e.g.* mineral oils such as liquid paraffin, *e.g.*, light or heavy petrolatum, petroleum jelly and petroleum wax (column 7, lines 11–12 and 26–30); and
- a surface-active agent of the cationic or amphoteric categories (column 7, lines 32–33) (Third Declaration of Christian Kropf, Paragraph 15).

(b) Ascertaining the differences between the prior art and the claims at issue

Claim 8 of the Kropf application is directed to a suspension. The remaining claims 9, 13-16 and 20-25 are directed to a toothpaste comprising the suspension, a method of remineralizing teeth comprising the suspension, or other suspensions within the scope of claim 8. Claim 8 reads as follows:

> Claim 8. A suspension of one or more phosphate calcium salts, fluoride calcium salts, or flurophosphate calcium salts in a liquid medium in which the salts are less than 1 g/l soluble, wherein the calcium salts comprise primary particles having diameters of from 5 to 50 nanometers and lengths of from 10 to 150 nanometers, stabilized against agglomeration by a content of at least 0.01% by weight, based on the weight of the suspension, of a water-soluble polymeric protective colloid selected from the group consisting of gelatin, casein, starch, plant gums, cellulose ethers, methylcellulose, hydroxyethylcellulose, carboxymethylcellulose, hydroxyethylstarch and hydroxypropyl guar, adsorbed onto said particles.

(Third Declaration of Christian Kropf, Paragraph 4).

A comparison of the suspension claimed in Claim 8 with the suspension disclosed in Rudin et al. reveals that the claimed suspension is distinct from the suspension taught or suggested by Rudin et al. Rudin et al. discloses crystals of pure hydroxyapatite of a defined particle size that are maintained in a suspension. Applicants' claimed suspension is of particles of calcium salts, wherein a defined water-soluble polymeric protective colloid, in particular, gelatin, is adsorbed onto said particles. Accordingly, Rudin et al. does not disclose or suggest Applicants' claimed suspension comprising particles of one or more calcium salts with a colloid (gelatin) adsorbed onto said particles, which is set forth in all of Applicants' pending claims 8-9, 13-16 and 20-25 (Third Declaration of Christian Kropf, Paragraph 10).

Baines et al. is directed to the pre-treatment of a milled alpha-alumina trihydrate abrasive in order that the abrasive does not react with and lessen the effectiveness of sodium fluoride in a dentifrice containing both the abrasive and sodium fluoride. Baines et al. does not

disclose either Applicants' claimed particles or water-soluble colloid. In other words, Baines et al. does not exemplify, disclose or suggest to one of ordinary skill in the art the use of treating materials selected from a water-soluble polymeric protective colloid selected from the group consisting of gelatin, casein, starch, plant gums, cellulose ethers, methylcellulose, hydroxyethylcellulose, carboxymethylcellulose, hydroxyethylstarch and hydroxypropyl guar (Third Declaration of Christian Kropf, Paragraph 16).

Baines et al. does not exemplify, disclose or suggest to one of ordinary skill in the art a suspension of one or more phosphate calcium salts, fluoride calcium salts, or fluorophosphate calcium salts in a liquid medium (Third Declaration of Christian Kropf, Paragraph 17).

Hence, the Baines et al. disclosure has very little materiality to Applicants' claimed invention.

(c) Resolving level of ordinary skill in pertinent art

The inventors of the present application, including Dr. Kropf, would represent persons of ordinary skill in the art.

(d) Possible utilization of secondary considerations

As set forth in *Graham v. John Deere Co.*:

> Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, *etc.*, might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented. As indicia of obviousness or nonobviousness, these inquiries may have relevancy.

(148 USPQ at 467).

As set forth above, Rudin et al. and Baines et al. have failed to discover, let alone exemplify, disclose or suggest to one of ordinary skill in the art Applicants' claimed suspension

comprising particles of calcium salt with a colloid as described in claim 8 adsorbed onto said particles (Third Declaration of Christian Kropf, Paragraph 18).

This failure of Rudin et al. and Baines et al. to discover Applicants' claimed suspension is not surprising as such failure is consistent with the teaching of Japanese Patent Document 6-329,557 to Oda et al. (English language translation), the prior art recited in the rejection of Applicants' claimed suspension in the United States Patent and Trademark Office Examiner's Action dated April 23, 2007.

Oda et al. relates to a carrier for absorbing a biologically active substance and medicinal preparation in which a biologically active substance is absorbed by this carrier (Paragraph [0001]). The Oda et al. invention is directed to a carrier for absorbing a biologically active substance comprising fine particles of hydroxyapatite with an average particle diameter of 500 nm or less surface-processed with albumin and/or a polyhydric organic acid (Paragraph [0006]) (Second Declaration of Christian Kropf, Paragraph 11).

In WORKING EXAMPLE 1 of Oda et al., fine particles of hydroxyapatite are surface treated with human serum albumin and low molecular weight gelatin in concentrations of 0.5 mg/ml, 1.5 mg/ml and 4.5 mg/ml (all aqueous solutions) (Paragraph [0017]). The dispersion of the surface-treated hydroxyapatite fine particles was measured using a granularity distribution measuring device (Shimazu Works) and the average particle diameter was determined. The effect of the human serum albumin and low molecular weight gelatin on the dispersion is shown in TABLE 1 on page 8 of the English text (Paragraphs [0018]–[0019], referenced in Paragraph 12 of the Second Declaration of Christian Kropf).

Oda et al. then discloses that according to the data set forth in TABLE 1, it is clear that the average particle diameter of the particles with human serum albumin was 100 nm or less, and that there was no aggregation and good dispersion properties no matter how much was added. When the low molecular weight gelatin was added, aggregation occurred and approximately 80% had an average particle diameter of 500 nm or more, no matter how much was added. (Second Declaration of Christian Kropf, Paragraph 13).

The result disclosed in Oda et al. teaches away from Applicants' claimed suspension of particles "stabilized against agglomeration by a content of at least 0.01% by weight, based on the weight of the suspension, of a water-soluble polymeric protective colloid selected from the group consisting of gelatin, casein, starch, plant gums, cellulose ethers, methylcellulose, hydroxyethylcellulose, carboxymethylcellulose, hydroxyethylstarch and hydroxypropyl guar, adsorbed onto said particles. In other words, Applicants' claimed suspension may include gelatin but does not include albumin or a polyhydric organic acid. In contrast, one of ordinary skill in the art of the subject matter of Applicants' invention relying on the teaching in Oda et al. that "when gelatin was added, aggregation occurred and approximately 80% had an average particle diameter of 500 nm or more no matter how much was added" would conclude that gelatin is unsuitable for stabilizing particles of hydroxyapatite against agglomeration.

Accordingly, one of ordinary skill in the art could not derive Applicants' claimed suspension of particles from Oda et al. (Second Declaration of Christian Kropf, Paragraph 14).In summary, Rudin et al. and Baines et al. fail to recognize, let alone exemplify, disclose or even suggest to one of ordinary skill in the art the suspension set forth in all of Applicants' claims 8–9, 12–16 and 20–25. In fact, Oda et al., the prior art previously relied on specifically teaches one of ordinary skill in the art that gelatin, a colloid claimed by Applicants, is unsuitable for stabilizing particles of hydroxyapatite against agglomeration. As noted above, claims 15–16, 20–21, 23 and 25 are specifically directed to the use of gelatin as the stabilizer, which is opposite to the teaching in Oda et al. Oda et al. illustrates the failure of others to recognize, let alone suggest, Applicants' claimed invention.

Accordingly, for the reasons set forth above, the rejection of claims 8–10, 13–17 and 20–21 under 35 U.S.C. Section 103(a) as being unpatentable over United States Patent No. 6,919,070 to Rudin et al. in view of United States Patent No. 4,098,878 to Baines et al. is untenable and should be withdrawn.

IV. Conclusion

It is believed that the above Amendment and Remarks constitute a complete response under 37 C.F.R. § 1.111 and that all bases of rejection in the Examiner's Action have been adequately rebutted or overcome. A Notice of Allowance in the next Office Action is, therefore, respectfully requested. The Examiner is requested to telephone the undersigned attorney if any matter that can be expected to be resolved in a telephone interview is believed to impede the allowance of pending claims 8-10, 13-16 and 20-25 of United States Patent Application Serial No. 09/868,379.

Respectfully submitted,

PAUL AND PAUL

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/John S. Child, Jr./
John S. Child, Jr.
Registration No. 28833
2000 Market Street
Suite 2900
Philadelphia, PA 19103-3229
Telephone: (215) 568-4900
Facsimile: (215) 567-5057
Attorneys for Applicants

CORRESPONDENCE ADDRESS
Customer No. 55495
Paul and Paul
2000 Market Street
Suite 2900
Philadelphia, PA 19103-3229
Paul and Paul Order No. 5835